SUMMARY OF THE CONFERENCE ON CARDIAC TRANSPLANTATION
DECEMBER 28, 1967 -- O'HARE AIRPORT, CHICAGO, ILLINOIS

Participants

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David M. Hume, M.D.
Adrian Kantrowitz, M.D.
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William P. Longmire, M.D.
Keith Reemstma, M.D.
Paul S. Russell, M.D.
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From the National Heart Institute:

Donald S. Fredrickson, M.D.
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Purpose

The purpose of the meeting was (1) to obtain an up-to-date assessment of the research activities in the field of cardiac transplantation; (2) to gain an assessment of how the first case of human cardiac transplantation would affect the plans that the American investigators might have for the extension of this experimental method to human application, particularly within the United States. The invited guests were all grantees of the National Institutes of Health; 13 were grantees of the National Heart Institute. Their fields of expertise included cardiovascular surgery, extracorporeal circulation, transplantation of the heart and of other organs, and the immunology of transplantation.

The participants discussed the topic and the framework of the following general questions:

(1) Do you anticipate performing a human cardiac transplant within the next year?

(2) What do you regard as the most critical logistical, technical or other scientific problems that require solution to make cardiac transplantation successful and to make it practical?

(3) What type of program assistance might the NIH provide that would materially accelerate the solution to those problems?

(4) Can you give us an estimate of cost of an individual transplant?

What is the cost to sustain your research program related to cardiac transplantation?

What might we anticipate to be the need for increased funds in the next several years relative to cardiac transplantation activities?

(5) How do you view the relationship of transplantation to:

(a) Development of mechanical circulatory assist devices?

(b) Development of the total implantable artificial heart?

Dr. Christiaan Barnard of Cape Town, South Africa -- the surgeon who supervised the team that performed the first human heart transplantation -- was invited to be present after it became apparent that his travel plans in the U.S.A. would permit it. Prior to the general discussion, Dr. Barnard related in detail many of the technical aspects of the operation that was performed on Mr. Washkansky. Several of the other surgeons asked for specific information concerning the operative techniques, the selection of the patient and the pharmacologic and therapeutic program in the postoperative period. The operative technique which was used was a modification of the procedure described by Dr. Norman Shumway of Stanford University. The program for immunosuppressive therapy was essentially that which is employed by Dr. David Hume and his team in kidney transplantation in Richmond, Virginia. In general it was clear that the techniques that were employed were directly derived from the experimental experience of the American surgical laboratories. Somewhat later in the program, aside from the general discussion as outlined, Dr. Adrian Kantrowitz of Maimonides Medical Center also discussed in some detail the technical aspects of the case which he performed two or three days after the operation in Cape Town. The operative technique used by Dr. Kantrowitz is also a modified Shumway procedure.

Summary of the Discussion

About half of the surgeons that were present felt that teams in their respective institutions would probably perform a cardiac transplant within the next year. There was an extensive discussion concerning the indications for the procedure. A variety of opinions were expressed on what types of patients constituted ideal recipients for a heart transplant. There was a general feeling that irrespective of the basic underlying pathology, if the fate of the patient was clearly established as being hopeless or terminal, the patient would be a suitable candidate (providing that the extracardiac systems of the patients were compatible with rehabilitation). The types of underlying pathology which were discussed included coronary heart disease, congenital heart disease, myopathies of infectious origin, and other unusual forms of heart disease.

Asked to consider among the following several problems:

(1) Pre-determination of tissue compatibilities

(2) Overcoming barriers to rapid access to cadaver hearts

(3) Organ preservations

(4) Maintenance of recipients immediately preceding transplant

(5) Transplantation itself

(6) Maintenance of recipients immediately following transplant

(7) Detection of rejection

(8) Suppression of immunologic rejection

(9) Understanding of the rejection phenomenon as related to cardiac tissue

Those present came to general agreement that the most crucial need for advancement lay in three categories.

1. Identified as the most important was the need for more fundamental understanding of the immunological problem.

2. There was unanimous agreement that there was need for better devices for mechanical circulatory support to allow for prolonged assistance of potential recipients and for maintenance of the donor heart during the intraoperative period.

3. The third principal area that was thought to need an acceleration of activity was work in the preservation of heart grafts. The availability of a banking or preservation and resuscitation procedure would allow more leeway in selecting and matching recipients with donors.

Other specific topics discussed in this context, but receiving less uniform endorsement, were concerned with developing more information on heterografting, or interspecies transplantation, the maintenance of animal colonies for this purpose, and for a specific program of drug or antilymphocyte serum development.

There was some concern among the guests that grant applications directed toward the problem of cardiac transplantation have not fared well in Study Section and Council reviews. There was extensive discussion on the reasons for this. Dr. Russell indicated that he felt that developments in immunology, at the present time, would now permit a more specific and directed approach to the problem of cardiac antigenicity and, therefore, the heart itself, as a transplanted organ, could now profitably be used as a test model. The subsequent discussion seemed to indicate that the impact of this first human transplant, and the new developments in immunology, would result in the capability of developing grant applications and protocols which would meet with more favorable review. In this context, it was also indicated that the ability to compete in this field would, of necessity, presume a broad-based team of experimentalists which could bring to bear a wide spectrum of expertise (particularly immunology) to the total problem.

It is of interest that the analysis from the Extramural Program Division of the National Heart Institute indicated that in the past fiscal year, the National Heart Institute supported 64 grants in the general field which had a total dollar value of $1,314,000. It was also pointed out that the National Institute for Allergy and Infectious Disease was supporting a center program for aid for investigators in problems of tissue typing. It was not clear to what extent the investigators in the field of transplantation of the heart were taking advantage of this service. It seemed that some were unaware of its availability or that the extent of possible aid from this source was not appreciated.

In further discussion of needs, it was clear that there is an acute shortage of scientific manpower for research in this area -- the most critical shortage being the availability of immunologists and immunochemists who would be able to devote the principal portion of their time to a coordinated study of the problem of transplantation of the heart. It was also pointed out that much of the immunological research in the transplantation field has been done under the aegis of certain departments of surgery. In polling the group, the opinions were expressed that a human case of cardiac transplantation would cost about $20,000. This does not include the cost beyond the early postoperative

period. There was a uniform feeling that there should be no crash program for financing clinical cardiac transplantation. However, the surgical scientists felt very strongly that the field would benefit from additional support, and that the experimental costs were very large.

Estimates of animal experiments in various centers ranged from $200 to $1200 per dog experiment. It was felt that an addition of about $150,000 per year to ongoing programs in experimental cardiac transplantation would be of great value to these workers. It was emphasized again that this work required a cohesive and broadly-based team. The procedure ought to be done by those who have had an extensive experimental background in the general fields of cardiovascular surgery, extracorporeal circulation, and transplantation biology.

A discussion of the relative roles of mechanical circulatory assistance and artificial hearts, and the cardiac replacement by a homograft, indicated that all the participants felt that these programs were intimately interdependent. Better pumps, better oxygenators and better systems for relatively long term circulatory support constitute critical needs. Comparisons were drawn between the impact that the developments in dialysis techniques have had upon the programs of kidney transplantation.

The statistical comparison of experimental success between the transplantation in the kidney and heart fields were made. It was emphasized that in the experimental situation at the present time, about two-thirds of animals undergoing experimental homotransplantation of the heart would survive the immediate operation, but only 20% would survive up to a month, with the current concepts of management. Other suggestions by the participants for furthering research efforts in this area included a suggested conference on the total problem of cardiac replacement. They emphasized that this conference should not be restricted to transplantation of the heart. They discussed a registry of patients who undergo replacement of the heart; and finally, spent some time on the discussion of the benefits of increasing communications in regional groups for developing ease in the detection, harvesting, and maintenance of donor organs.